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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,179	09/09/2003	John Joseph Deadman	6613-66764	7468
24197	7590	06/15/2005	EXAMINER	
KLARQUIST SPARKMAN, LLP 121 SW SALMON STREET SUITE 1600 PORTLAND, OR 97204			CORDERO GARCIA, MARCELA M	
			ART UNIT	PAPER NUMBER
			1654	

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,179	DEADMAN ET AL.	
	Examiner	Art Unit	
	Marcela M Cordero Garcia	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 22-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 and 28-40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. <u>05/05</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/4, 3/4, 8/4 & 10/4</u> | 6) <input type="checkbox"/> Other: _____ |

RD

DETAILED ACTION

The restriction requirement presented in the Office Action of February 18, 2005 was missing claims 22-23. Therefore this restriction is vacated and replaced by the following one:

- I. Claims 1-11 and 20, drawn to an organoboronic acid salt, classified, e.g., in class 514, subclass 64.
- II. Claims 12-19, drawn to a salt of a boronic acid of formula (IV), classified, e.g., in class 514, subclass 19.
- III. Claims 21 and 24-26, drawn to a salt of a boronic acid of formula (III), classified, e.g., in class 546, subclass 13.
- IV. Claim 27, drawn to a method of making a salt of a boronic acid of formula (IV), classified, e.g., in class 514, subclass 19.
- V. Claims 22-23, drawn to a method of using an organoboronic acid salt, classified, e.g., in class 514, subclass 64.

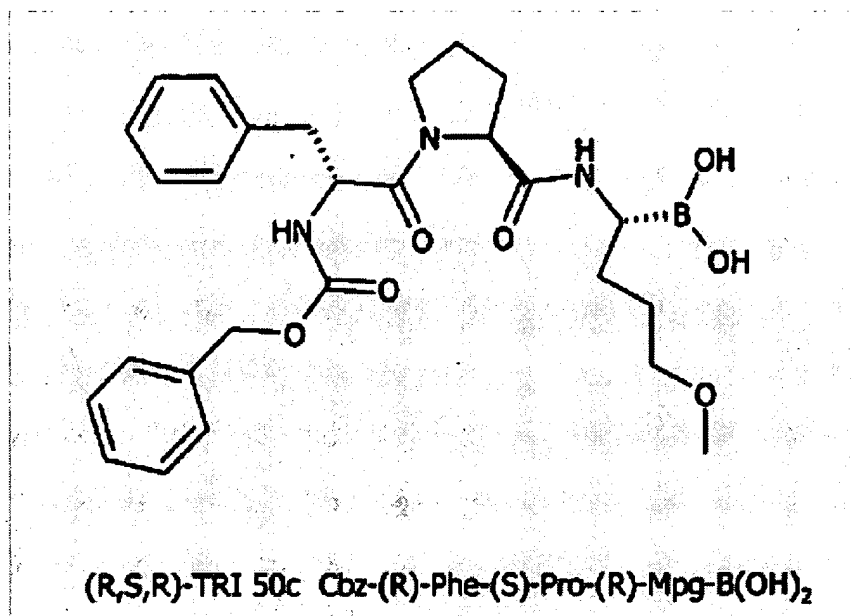
During a telephonic interview on June 9, 2005 explaining the aforementioned information, Applicant's representative still elects Group I as stated in the response to the restriction requirement mailed on March 21, 2005.

Acknowledgement is therefore made of Applicant's election of Group I, claims 1-21, and new claims 28-40 in the response of March 21, 2005. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

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In addition, Applicant's election of the following species is acknowledged:

The hemicalcium salt of Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)₂ [also known as (R,S,R)-TRI 50c], which has the chemical formula as indicated below:



Claims 22-27 are not drawn to the elected Group, and therefore are withdrawn.

Claims 1-21 and new claims 28-40 (Group I) are presented for examination on the merits to the extent that they read upon the elected species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been

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obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-21 and 28-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deadman et al. (J Med Chem 1995) in view of Skordalakes et al (J Am Chem, 1997).

Deadman et al. beneficially teach an organoboronic acid pinacol ester inhibitor of thrombin having a neutral thrombin S1-binding moiety linked to a hydrophobic thrombin S2/S3-binding moiety. (See, e.g., page 1514, Table 5, species 9a).

Deadman et al. do not specifically teach the organoboronic acid hemicalcium salt thereof.

Skordalakes et al. (J Am Chem Soc, 1997) beneficially teach analogous organoboronic acid inhibitors that are non-pinacolic (see, e.g., Figure 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust particular conventional working conditions within such compositions (e.g., using specifically boronic acid salts such as hemicalcium) based upon the overall beneficial teachings provided by Deadman et al. indicating that the compound of page 1514, species 9a, which is the pinacol

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ester of the elected species, was one of the best inhibitors from amongst similar compounds (page 1513, lines 8-9) and the beneficial teachings of Skordalkes et al. describing analogous boronic acid (non-pinacolic) inhibitors (see, e.g., Figure 1 and page 9936, last paragraph) because there was an increased interest in the development of new, low molecular weight inhibitors of thrombin to replace the existing ones (See, e.g., Deadman et al., page 1511, lines 1-21 and Skordalakes et al., page 9936, last paragraph). These types of adjustments are deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of evidence to the contrary.

Claims 1-21 and 28-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claeson et al. (Biochem J, 1993) in view of Skordalakes et al. (J Am Chem Soc, 1997).

Claeson et al. beneficially teach an organoboronic acid pinanediol ester inhibitor of thrombin having a neutral thrombin S1-binding moiety linked to a hydrophobic thrombinS2/S3-binding moiety. (See, e.g., abstract).

Claeson et al. do not specifically teach the hemicalcium salt of the organoboronic acid thereof.

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Skordalakes et al. (J Am Chem Soc, 1997) beneficially teach analogous non-pinenediol ester organoboronic acid inhibitors (see, e.g., Figure 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust particular conventional working conditions within such compositions (e.g., using specifically boronic acid salts such as hemicalcium) based upon the overall beneficial teachings provided by Claeson et al. indicating that the compound of page 310, scheme 1, figure IV, which is the pinenediol ester of the elected species, was a potent inhibitor of thrombin (see, e.g., page 309, abstract) and the beneficial teachings of Skordalakes et al. describing analogous boronic acid (non-pinenediolic) inhibitors (see, e.g., Figure 1 and page 9936, last paragraph) because there was an increased interest in developing new low molecular weight inhibitors of thrombin having fewer side effects than those available (See, e.g., Claeson et al., page 311, column 2, paragraph 2 & page 312 and Skordalakes et al., page 9936, last paragraph). These types of adjustments are deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re*

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Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-21 and new claims 28-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 28-38 of copending Application No. 11/078,097. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims stated above are drawn to the same species hemicalcium salt of Cbz -(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)₂. Therefore, claims 28-38 of Application '097 encompass or are encompassed by the instant claims 1-21 and 28-40.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-21 and new claims 28-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 and 50-58 of copending Application No. 10/659,178. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims stated above are drawn to

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the same species hemicalcium salt of Cbz -(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)₂.

Therefore, claims 1-24 and 50-58 of Application '178 encompass or are encompassed by the instant claims 1-21 and 28-40.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Information Disclosure Statement

The information disclosure statements (IDSs) submitted on 02/24/2004, 03/18/2004, 08/23/2004 and 10/20/2004 were filed after the mailing date of the application on 09/09/2003. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

However, please also note that the patent applications cited on the IDS communication of 5/27/2005, although considered, do not constitute proper citable references on an IDS as no PTO 1449 was provided and therefore the IDS of 5/27/05 has not been initialed by the Examiner.

Conclusion

No claim is allowed.

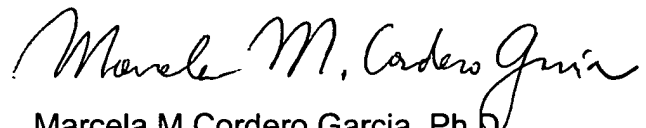
The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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Patent Examiner
Art Unit 1654

MMCG 06/05



CHRISTOPHER R. TATE
PRIMARY EXAMINER